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10/576,733

04/21/2006

Ian Taylor

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35969

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05/15/2008

Bayer Health Care LLC
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West Haven, CT 06516

EXAMINER

CANELLA, KAREN A

ART UNIT

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1643

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--------------------------------------|--------------------------------------|--|
| Office Action Summary | Application No. 10/576,733 | Applicant(s) TAYLOR ET AL. | |
| | Examiner Karen A. Canella | Art Unit 1643 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-25 is/are pending in the application.
4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-25 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

Claims 1-25 are pending and examined on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 20 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of anti-cancer agent in claim 20 lacks antecedent basis in claim 19.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 25 is rejected under 35 U.S.C. 102(b) as being anticipated by Zhang et al (Journal of Biological Chemistry, October 18, 2002, Vol. 272, pp. 39379-39387).

Claim 25 is drawn to a kit comprising a primary antibody directed to pERK, a secondary antibody, reagents, reference and control samples.

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Zhang et al disclose a primary rabbit antibody that binds to phosphorylated p42/44 mitogen-activated protein kinase, untreated PDK1 -/- ES cells, untreated wild-type ES cells and treated wild-type ES cells (legend for figure 4) which fulfills the limitations of reference samples and control samples. Phosphorylated p42/44 mitogen-activated protein kinase is a phosphorylated extracellular signal-regulated kinase (pERK). Zhang et al disclose a goat anti-rabbit secondary antibody conjugated to horseradish peroxidase and visualized using the chemiluminescence Western detection kit, which fulfills the specific embodiments of a secondary antibody and reagents.

Claims 1, 3-19, 21-24 are rejected under 35 U.S.C. 102(e) as being anticipated by Bacus (U.S. 2003/0045451).

Claims 1, 7, 12 and 15 are drawn to a method comprising determining the level of expression of one or more proteins in a first biological sample taken from a patient prior to treatment with an anti-cancer agent and determining the level of expression of one or more proteins in at least a second biological sample taken from the patient subsequent to treatment with an anti-cancer agent.

Claim 19 is drawn to a method comprising determining the level of expression of one or more proteins in a first biological sample taken from a patient and comparing the level of expression to the level of one or more proteins in a second biological samples taken from a normal patient sample

Claims 3, 8, 13, 16 and 21 embody the methods of claims 1, 7, 12, 15 and 19, respectively, wherein said protein is pERK.

Claims 4, 9, 18 and 22 embody the methods of claims 1, 7, 15 and 19, respectively, wherein said cancer is selected from a list including breast cancer.

Claims 5, 10, 14, 17, and 23 embody the methods of claims 1, 7, 12, 15, and 19, respectively, wherein the protein expression level is assessed by immunohistochemistry.

Claims 6, 11 and 24 embody the methods of claims 1, 7, and 19, wherein the sample is a tumor biopsy.

Bacus discloses a method comprising obtaining a first tissue or cell sample from an individual prior to exposure to a therapeutic agent; obtaining a second tissue or cell sample from

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said individual after exposure to a therapeutic agent, and comparing the amount of one or a plurality of biological makers in said first and second tissue sample (claim 1). The disclosure of a cell or tissue sample from an individual fulfills the specific embodiment of a biopsy. Bacus discloses that the amount of one or a plurality of biological markers is determined immunohistochemically (claim 6). Bacus discloses the detection of pERK as a marker [0085, line 9], thus fulfilling the requirements of claims 3, 8, 13, 16 and 21. Bacus disclose samples taken from breast and bladder [0097 and 0098].

It is noted that the recitation of a method for “monitoring the response of a patient”, “providing diagnosis of cancer”, “distinguishing between normal and disease tissues”, “discovering novel drugs”, and “selecting patients eligible for anti-cancer treatment” has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

Phrases such as “comparing the level of expression” are also without patentable weight as these are mental steps rather than active, tangible steps.

It is further noted that the phrase “wherein a change in the level of expression” is not given patentable weight when comparing the claims to the prior art as it simply expresses the intended result of a process step positively recited, see MPEP 2111.04.

Given that the method of the prior art comprises the same method steps as claimed in the instant invention, the claimed method is anticipated because the method will inherently be a method for identifying a compound that modulates the cell cycle. See *Ex parte Novitski* 26 USPQ 1389 (BPAI 1993).

Claims 1-3, 7, 8, 12, 13, 15, 16, 19-21 are rejected under 35 U.S.C. 102(b) as being anticipated by the abstract of Hedley et al (Clinical Cancer Research, November 2001, Vol. 7, No. 11, suppl, pp. 3712S-3712S).

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The abstract of Hedley et al discloses a method comprising taking a sample of blood cells from a patient before treatment with BAY 43-9006, a Raf-kinase inhibitor, followed by taking a blood sample from patients 1, 2, 4, 8, 12 and 24 hours after the first and last doses of BAY 46-9006, wherein ERK1/2 activation is measured. the abstract discloses that the results are compared to that of healthy persons which meets the limitations of claims 19-21.

It is noted that the recitation of a method for “monitoring the response of a patient”, “providing diagnosis of cancer”, “distinguishing between normal and disease tissues”, “discovering novel drugs”, and “selecting patients eligible for anti-cancer treatment” has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

Phrases such as “comparing the level of expression” are also without patentable weight as these are mental steps rather than active, tangible steps.

It is further noted that the phrase “wherein a change in the level of expression” is not given patentable weight when comparing the claims to the prior art as it simply expresses the intended result of a process step positively recited, see MPEP 2111.04.

Given that the method of the prior art comprises the same method steps as claimed in the instant invention, the claimed method is anticipated because the method will inherently be a method for identifying a compound that modulates the cell cycle. See *Ex parte Novitski* 26 USPQ 1389 (BPAI 1993).

Claims 1, 4-7, 9-12, 14, 15, 17-19, 22-24 are rejected under 35 U.S.C. 102(e) as being anticipated by Taylor et al (WO 2005/032495).

Taylor et al disclose a method comprising (a) determining the level of expression of one or more genes or gene products in a first biological sample taken from the patient; (b) determining the level of expression of one or more genes or gene products in at least a second biological sample taken from a normal patient sample (claims 1-6) which fulfills the instant

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embodiments of claim 19 and a method comprising (a) determining the level of expression of one or more genes or gene products in a first biological sample taken from the patient prior to treatment with the anti-cancer agent; (b) determining the level of expression of one or more genes or gene products in at least a second biological sample taken from the patient subsequent to the treatment with the anti-cancer agent (claims 7-12) which fulfills the limitations of claims 1, 7, 12 and 15. Taylor et al disclose biological samples which are tumor biopsies [018] and cancers selected from the group consisting of solid tumors, such as cancers of the breast, respiratory tract, brain, reproductive organs, digestive tract, urinary tract, eye, liver, skin, head and neck, thyroid, parathyroid, and their distant metastases, as well as lymphomas, sarcomas, and leukemias [049]. Taylor et al disclose detection of proteins by immunohistochemical methods [148].

It is noted that the recitation of a method for “monitoring the response of a patient”, “providing diagnosis of cancer”, “distinguishing between normal and disease tissues”, “discovering novel drugs”, and “selecting patients eligible for anti-cancer treatment” has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

Phrases such as “comparing the level of expression” are also without patentable weight as these are mental steps rather than active, tangible steps.

It is further noted that the phrase “wherein a change in the level of expression” is not given patentable weight when comparing the claims to the prior art as it simply expresses the intended result of a process step positively recited, see MPEP 2111.04.

Given that the method of the prior art comprises the same method steps as claimed in the instant invention, the claimed method is anticipated because the method will inherently be a method for identifying a compound that modulates the cell cycle. See *Ex parte Novitski* 26 USPQ 1389 (BPAI 1993).

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Claims 1, 2, 4-6, 15, 17, 18 are rejected under 35 U.S.C. 102(e) as being anticipated by Everleigh et al (U.S. 2004/0121375).

Everleigh et al disclose a method comprising (a) determining the level of expression of one or more one biomarker(s) in a first biological sample taken from the patient prior to treatment with the anti-cancer agent; (b) determining the level of expression of the biomarker in at least a second biological sample taken from the patient subsequent to the initial treatment with the anti-cancer agent (claims 1, 6 and 8) Everleigh et al disclose that samples can be obtained through biopsy (claim 5) and that cancers include solid tumors, such as cancers of the breast, respiratory tract, brain, reproductive organs, digestive tract, urinary tract, eye, liver, skin, head and neck, thyroid, parathyroid, and their distant metastases, as well as lymphomas, sarcomas, and leukemias [0045 and claim 2]. Everleigh et al disclose that the biomarkers are detected by immunohistochemical analysis [0120] and that the anti-cancer agent is a raf kinase inhibitor (claim 3).

It is noted that the recitation of a method for “monitoring the response of a patient”, “providing diagnosis of cancer”, “distinguishing between normal and disease tissues”, “discovering novel drugs”, and “selecting patients eligible for anti-cancer treatment” has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

Phrases such as “comparing the level of expression” are also without patentable weight as these are mental steps rather than active, tangible steps.

It is further noted that the phrase “wherein a change in the level of expression” is not given patentable weight when comparing the claims to the prior art as it simply expresses the intended result of a process step positively recited, see MPEP 2111.04.

Given that the method of the prior art comprises the same method steps as claimed in the instant invention, the claimed method is anticipated because the method will inherently be a

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method for identifying a compound that modulates the cell cycle. See Ex parte Novitski 26 USPQ 1389 (BPAI 1993).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 7, 12, 15 and 19 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 4-6, 8-10, 12, 13 and 15 of copending Application No. 10/581,213. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the ‘213 application

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anticipate the instant claims to the extent that they encompass determination of the level of expression of one or more gene products which are polypeptides..

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1 and 15 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-18 of copending Application No. 10/581,125. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '125 application anticipate the instant claims to the extent that they encompass determination of the level of expression of one or more biomarkers which are polypeptides..

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 2, 4, 6, 15 and 18 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-18 of copending Application No. 11/589,295. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '295 application anticipate the instant claims. It is noted that sorafenib is synonymous with BAY 43-9006, which is a raf-kinase inhibitor.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 2, 4, 6, 7, 9, 11, 12, 15, 18, 19, 20, 22 and 24 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3, 5-7, 27, 28-50 of copending Application No. 11/589,824. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '824 application anticipate the instant claims. It is noted that sorafenib is synonymous with BAY 43-9006, and the structure of illustrated in claim 47 of the '824 application, and that BAY 43-9006 is a raf-kinase inhibitor.

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This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 2, 4, 6, 15 and 18 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3, 5-7, 27, 28-50 of copending Application No. 10/675,406. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '406 application anticipate the instant claims to the extent that the biomarkers of claims 1, 2 and 5 and the gene products of claims 6-9 are polypeptides.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

All claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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/Karen A Canella/

Primary Examiner, Art Unit 1643